

=> d his

(FILE 'HOME' ENTERED AT 10:16:56 ON 11 APR 2005)

FILE 'CAPLUS' ENTERED AT 10:17:44 ON 11 APR 2005  
E US6624197/PN

L1 4 S E3  
SELECT RN L1 1

L2 FILE 'REGISTRY' ENTERED AT 10:18:54 ON 11 APR 2005  
10 S E1-E10

L3 FILE 'REGISTRY' ENTERED AT 10:24:49 ON 11 APR 2005  
STRUCTURE UPLOADED

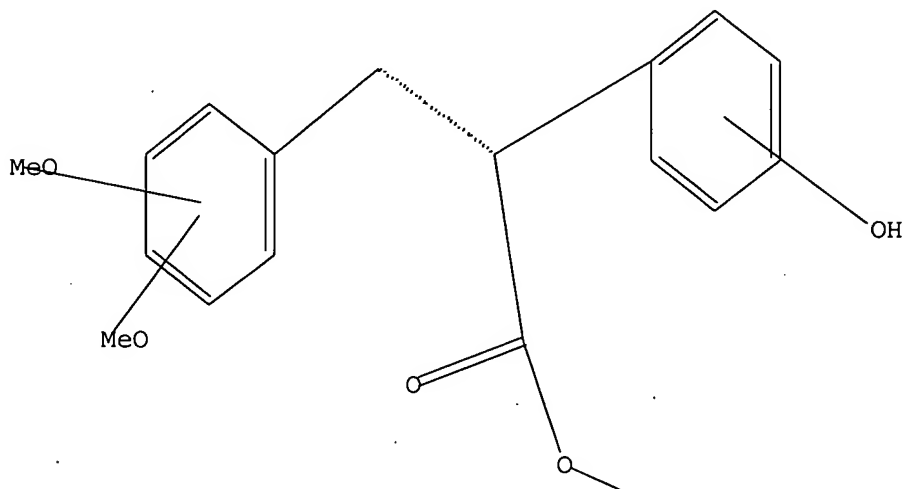
L4 1 S L3  
L5 10 S L3 FUL

L6 FILE 'CAPLUS' ENTERED AT 10:25:20 ON 11 APR 2005  
11 S L5

=> d 13

L3 HAS NO ANSWERS

L3 STR



Structure attributes must be viewed using STN Express query preparation.

=> d bib abs hitstr 1-11

L6 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2004:75190 CAPLUS  
DN 140:321127  
TI A new short synthesis of coumestrol and its application for the synthesis  
of [6,6a,11a-13C3]coumestrol  
AU Al-Maharik, Nawaf; Botting, Nigel P.  
CS School of Chemistry, University of St Andrews, St Andrews, Fife, KY16 9ST,  
UK  
SO Tetrahedron (2004), 60(7), 1637-1642  
CODEN: TETRAB; ISSN: 0040-4020  
PB Elsevier Science B.V.  
DT Journal  
LA English  
AB A convenient and simple two-step method for the synthesis of coumestrol

has been established, which involves a base catalyzed condensation of Ph acetate with benzoyl chloride, followed by demethylation and subsequent tandem intramol. cyclization. This method was then employed for the efficient synthesis of multiply <sup>13</sup>C-labeled coumestrol.

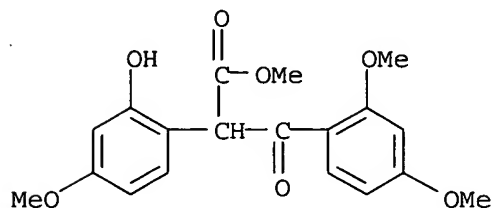
IT 677717-62-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of coumestrol and [6,6a,11a-<sup>13</sup>C<sub>3</sub>]coumestrol)

RN 677717-62-3 CAPLUS

CN Benzenepropanoic acid, α-(2-hydroxy-4-methoxyphenyl)-2,4-dimethoxy-β-oxo-, methyl ester (9CI) (CA INDEX NAME)



RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:757334 CAPLUS

DN 139:276885

TI Preparation of novel heterocyclic analogs of diphenylethylene compounds as antidiabetics

IN Neogi, Partha; Dey, Debendranath; Medicherla, Satyanarayana; Nag, Bishwajit; Lee, Arthur

PA USA

SO U.S. Pat. Appl. Publ., 66 pp., Cont.-in-part of U.S. Ser. No. 843,167.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003181494	A1	20030925	US 2002-265902	20021008
	US 2002025975	A1	20020228	US 2001-785554	20010220
	US 2002032225	A1	20020314	US 2001-843167	20010427
	WO 2004033438	A1	20040422	WO 2003-US31803	20031008
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 1999-287237	A2	19990406		
	US 2000-591105	B2	20000609		
	US 2001-785554	A2	20010220		
	US 2001-843167	A2	20010427		
	US 1998-74925	A2	19980508		
	US 2002-265902	A2	20021008		

OS MARPAT 139:276885

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The title compds. [I; Z = II-IV; n, m, q and r = 0-4 (n+m ≤ 4 and q+r ≤ 4); p, s = 0-5 (p+s ≤ 5); R, R2 = H, alkyl, alkenyl, etc.; R1 = H, alkyl, alkenyl, etc.; A, A1, A2 = H, acylamino, acyloxy, alkanoyl, etc.; B, B1, B2 = H, acylamino, acyloxy, alkanoyl, etc.; or A and B together, or A1 and B1 together, or A2 and B2 together, may be joined to form a methylenedioxy or ethylenedioxy; X, X1 = (un)substituted NH, O, S] which are effective in lowering blood glucose level, serum insulin, triglyceride and free fatty acid levels in animal models of Type II diabetes, were prepared. E.g., a multi-step synthesis of V, starting from 3,5-dimethoxybenzaldehyde and 4-hydroxyphenylacetic acid, was given. The compound V showed strong glucose lowering activity even though it is a weak PPAR-γ agonist (data given). The compds. I are disclosed as useful for a variety of treatments including the treatment of inflammation, inflammatory and immunol. diseases, insulin resistance, hyperlipidemia, coronary artery disease, cancer and multiple sclerosis. Pharmaceutical composition comprising the compound I was claimed.

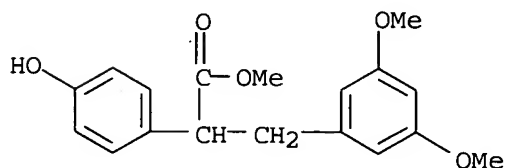
IT 380881-43-6P 606932-78-9P 606932-85-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of diphenylethylene compds. containing thiazolidinedione or oxazolidinedione moieties for treating diabetes, inflammatory or immunol. disease in combination with other agents)

RN 380881-43-6 CAPLUS

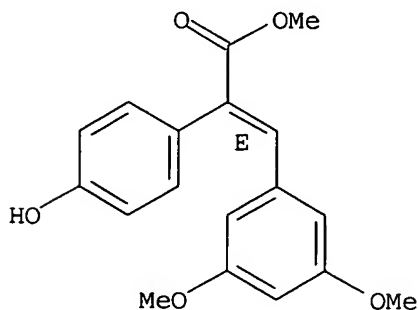
CN Benzenepropanoic acid, α-(4-hydroxyphenyl)-3,5-dimethoxy-, methyl ester (9CI) (CA INDEX NAME)



RN 606932-78-9 CAPLUS

CN Benzenecarboxylic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-hydroxy-, methyl ester, (αE)- (9CI) (CA INDEX NAME)

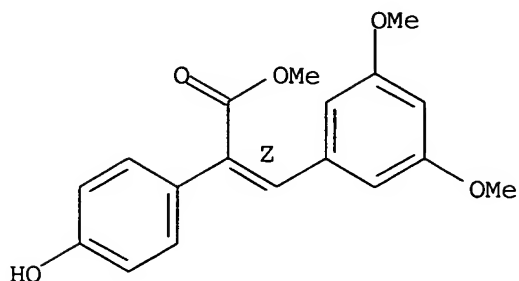
Double bond geometry as shown.



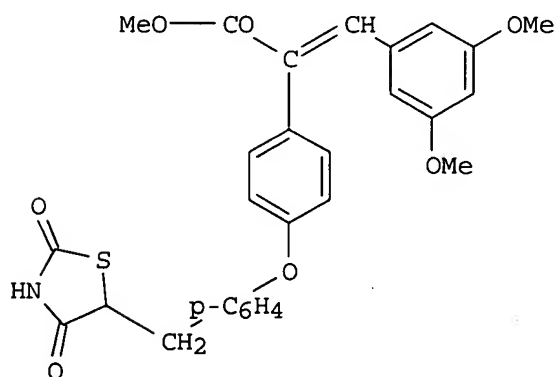
RN 606932-85-8 CAPLUS

CN Benzenecarboxylic acid, α-[(3,5-dimethoxyphenyl)methylene]-4-hydroxy-, methyl ester, (αZ)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L6 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2003:645701 CAPLUS  
 DN 140:87046  
 TI Synthesis and structure-Activity relationship studies of cinnamic acid-based novel thiazolidinedione antihyperglycemic agents  
 AU Neogi, Partha; Lakner, Fredrick J.; Medicherla, Satyanarayana; Cheng, Jin; Dey, Debendranath; Gowri, Maya; Nag, Bishwajit; Sharma, Somesh D.; Pickford, Lesley B.; Gross, Coleman  
 CS Department of Chemistry, Calyx Therapeutics Inc., Hayward, CA, 94545, USA  
 SO Bioorganic & Medicinal Chemistry (2003), 11(18), 4059-4067  
 CODEN: BMECEP; ISSN: 0968-0896  
 PB Elsevier Science Ltd.  
 DT Journal  
 LA English  
 OS CASREACT 140:87046  
 GI



I

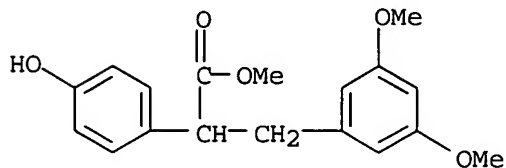
AB A number of 2,4-thiazolidinedione derivs. of -Ph substituted cinnamic acid were synthesized and studied for their PPAR agonist activity. The E-isomer of cinnamic acid, I, showed moderate PPAR transactivation. The corresponding Z-isomer and double bond reduced derivative were found to be much less potent. Although the E-isomer showed a moderate PPARy transactivation, it demonstrated a strong glucose-lowering effect in a genetic rodent model of diabetes. Results of pharmacokinetic, metabolism and permeability studies are consistent with I being an active prodrug with the hydrolyzed carboxylate as an active metabolite that has similar glucose lowering and PPARy agonist properties.  
 IT 380881-43-6P 606932-78-9P 606932-85-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(cinnamic acid-based thiazolidinedione antihyperglycemic agents)

RN 380881-43-6 CAPLUS

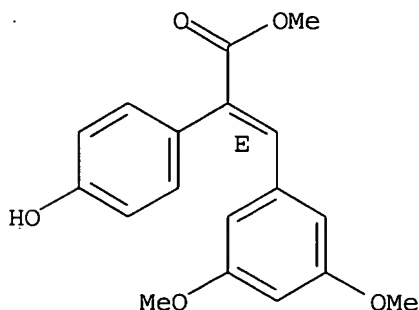
CN Benzenepropanoic acid,  $\alpha$ -(4-hydroxyphenyl)-3,5-dimethoxy-, methyl ester (9CI) (CA INDEX NAME)



RN 606932-78-9 CAPLUS

CN Benzeneacetic acid,  $\alpha$ -[(3,5-dimethoxyphenyl)methylene]-4-hydroxy-, methyl ester, ( $\alpha$ E)- (9CI) (CA INDEX NAME)

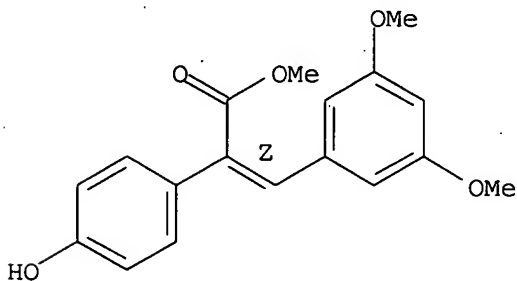
Double bond geometry as shown.



RN 606932-85-8 CAPLUS

CN Benzeneacetic acid,  $\alpha$ -[(3,5-dimethoxyphenyl)methylene]-4-hydroxy-, methyl ester, ( $\alpha$ Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:185699 CAPLUS

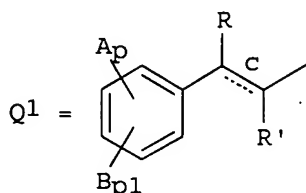
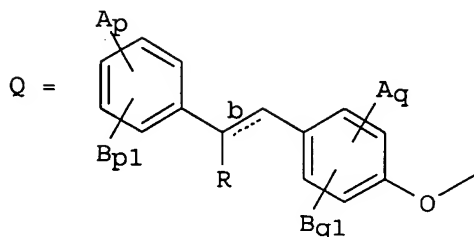
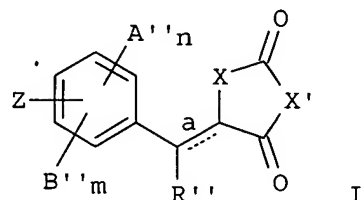
DN 136:247571

TI Preparation of novel heterocyclic analogs of diphenylethylene compounds as inhibitors of cytokines or cyclooxygenase

IN Nag, Bishwajit; Dey, Debendranath; Medicherla, Satyanarayana; Neogi, Partha

PA USA  
 SO U.S. Pat. Appl. Publ., 34 pp., Cont.-in-part of U.S. Ser. No. 785,554.  
 CODEN: USXXCO  
 DT Patent  
 LA English  
 FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002032225	A1	20020314	US 2001-843167	20010427
	US 6245814	B1	20010612	US 1998-74925	19980508
	US 2002025975	A1	20020228	US 2001-785554	20010220
	CA 2410171	AA	20011220	CA 2001-2410171	20010605
	WO 2001095859	A2	20011220	WO 2001-US17950	20010605
	WO 2001095859	A3	20030828		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU	2001066670	A5	20011224	AU 2001-66670	20010605
EP	1360178	A2	20031112	EP 2001-944241	20010605
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
JP	2004527455	T2	20040909	JP 2002-510041	20010605
US	2003181494	A1	20030925	US 2002-265902	20021008
US	2004186299	A1	20040923	US 2004-808519	20040325
PRAI	US 1998-74925	A2	19980508		
	US 1999-287237	A2	19990406		
	US 2000-591105	A2	20000609		
	US 2001-785554	A2	20010220		
	US 2001-843167	A	20010427		
	WO 2001-US17950	W	20010605		
OS	MARPAT 136:247571				
GI					



AB Novel diphenylethylene compds. and derivs. thereof containing thiazolidinedione or oxazolidinedione moieties are provided which are

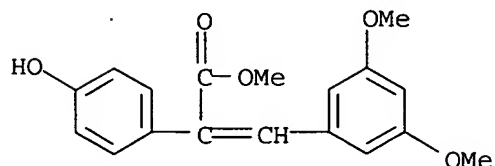
effective in lowering blood glucose level, serum insulin, triglyceride and free fatty acid levels in animal models of Type II diabetes. The above compds. and their derivs. are resented by formula [I; Z = Q, Q1, H, A", B"; wherein n, m, q, q1 = integers from zero to 4 provided that  $n+m \leq 4$  and  $q+q1 \leq 4$ ; p, p1 = integers from zero to 5 provided that  $p+p1 \leq 5$ ; a, b and c are double bonds which may be present or absent; when present; the double bonds may be in the E or Z configuration and, when absent, the resulting stereocenters may have the R- or S- configuration; R, R', R" = H, C1-20 linear or branched alkyl, C2-20 linear or branched alkenyl, CO2Z' (wherein Z' = H, Na, K, or other pharmaceutically acceptable counterion such as Ca, Mg, ammonium, tromethamine, and the like), CO2R''', NH2, NHR''', N(R''')2, OH, OR''', halo, substituted C1-20 linear or branched alkyl or substituted C2-20 linear or branched alkenyl (wherein R''' is C1-20 linear or branched alkyl or linear or branched alkenyl); A, A', A'' = H, C1-20 acylamino, C1-20 acyloxy, C1-20 alkanoyl, C1-20 alkoxycarbonyl, C1-20 alkoxy, C1-20 alkylamino, C1-20 alkylcarboxylamino, CO2H, cyano, halo, HO; B, B', B'' = H, C1-20 acylamino, C1-20 acyloxy, C1-20 alkanoyl, C1-20 alkenoyl, C1-20 alkoxycarbonyl, C1-20 alkoxy, C1-20 alkylamino, C1-20 alkylcarboxylamino, aroyl, aralkanoyl, CO2H, cyano, halo, HO; or A and B together, or A' and B' together, or A'' and B'' together, may be joined to form a methylenedioxy or ethylenedioxy group; and X, X' are independently -NH, -NR''', O or S]. In contrast to previously reported thiazolidinedione compds., known to lower leptin levels, the present compds. increase leptin levels and have no known liver toxicity. They inhibit the activity of TNF-alpha, interleukin IL-1 or IL-6 or cyclooxygenase-2 (COX-2). The compds. are disclosed as useful for a variety of treatments including the treatment of inflammation, inflammatory and immunol. diseases, insulin resistance, hyperlipidemia, coronary artery disease, cancer and multiple sclerosis. Thus, To a mixture of 3,5-dimethoxybenzaldehyde (500 g) and p-hydroxyphenylacetic acid (457 g) was added acetic anhydride (1 L) and triethylamine (420 mL) and the nonhomogeneous mixture on heating became homogeneous at 70° and stirred at 130-140° for 6 h to give 47% 3-(3,5-dimethoxyphenyl)-2-(4-hydroxyphenyl)acrylic acid (II) (428 g). II (427.5 g) was suspended in 3 L methanol, treated with 100 mL concentrated H2SO4, and heated at reflux for 20 h under Ar to give 97% 3-(3,5-dimethoxyphenyl)-2-(4-hydroxyphenyl)acrylic acid Me ester (III). III (433 g) was dissolved in 1.6 L DMF, treated with 60.4 g NaH (50% in oil) and the with 185 mL p-fluorobenzaldehyde, and heated at 180° for 18 h to give 77% 3-(3,5-dimethoxyphenyl)-2-[4-(4-formylphenoxy)phenyl]acrylic acid Me ester which (352 g), 2,4-thiazolidinedione 98.6, benzoic acid 134, and piperidine 107.4 g were heated in 2.5 L toluene at reflux with continuous removal of H2O through Dean-Stark apparatus to give 86% 3-(3,5-dimethoxyphenyl)-2-[4-[4-(2,4-dioxothiazolidin-5-ylidenemethyl)phenoxy]phenyl]acrylic acid Me ester (IV). IV (30 g) was hydrogenated over 15 g 10% Pd-C in 900 mL dioxane in a Parr apparatus at 60 Psi for 24 h, followed by adding 15 g 10% Pd-C and continuing the hydrogenation for another 24 h to give 86% 3-(3,5-dimethoxyphenyl)-2-[4-[4-(2,4-dioxothiazolidin-5-ylmethyl)phenoxy]phenyl]acrylic acid Me ester (V). When V was orally administered to ob/ob mice with a single oral dose (50 mg/kg body weight), there was a 62 % drop in blood glucose level and, similar to db/db mice, there was no significant increase in body weight between the control and the treatment groups. This was in contrast to treatment of diabetic animals by thiazolidinedione type compds. which are known to be associated with increase in body weight

IT **380881-27-6P**, 3-(3,5-Dimethoxyphenyl)-2-(4-hydroxyphenyl)acrylic acid methyl ester

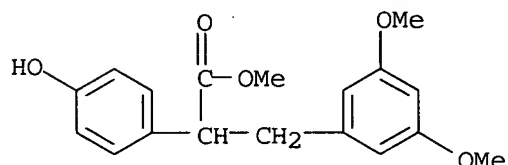
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of novel heterocyclic analogs of phenylethylene compds. as inhibitors of cytokines or cyclooxygenase for therapeutic agents)

RN 380881-27-6 CAPLUS  
 CN Benzenecetic acid,  $\alpha$ -[(3,5-dimethoxyphenyl)methylene]-4-hydroxy-,  
 methyl ester (9CI) (CA INDEX NAME)



IT **380881-43-6P**, 3-(3,5-Dimethoxyphenyl)-2-(4-hydroxyphenyl)propionic  
 acid methyl ester  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (intermediate; preparation of novel heterocyclic analogs of phenylethylene  
 compds. as inhibitors of cytokines or cyclooxygenase for therapeutic  
 agents)  
 RN 380881-43-6 CAPLUS  
 CN Benzenepropanoic acid,  $\alpha$ -(4-hydroxyphenyl)-3,5-dimethoxy-, methyl  
 ester (9CI) (CA INDEX NAME)

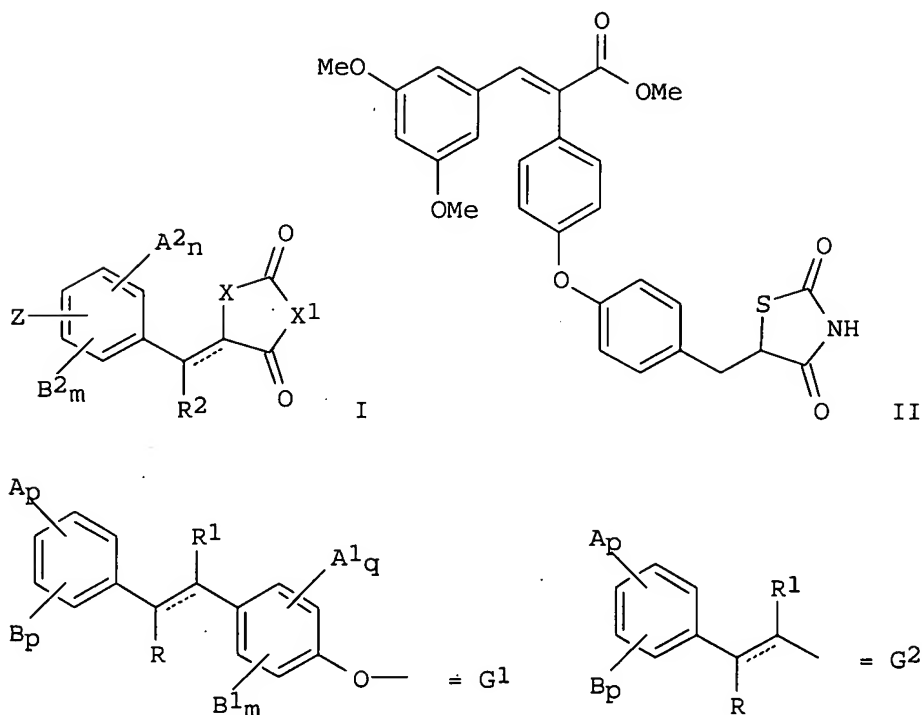


L6 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2002:158391 CAPLUS  
 DN 136:216745  
 TI Preparation and activity of diphenylethylene thiazolidinediones and  
 analogs as antidiabetics, antiinflammatories, or immunomodulators  
 IN Nag, Bishwajit; Dey, Debendranath; Medicherla, Satyanarayana; Neogi,  
 Partha  
 PA USA  
 SO U.S. Pat. Appl. Publ., 30 pp., Cont.-in-part of U.S. Ser. No. 591,105.  
 CODEN: USXXCO  
 DT Patent  
 LA English  
 FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002025975	A1	20020228	US 2001-785554	20010220
	US 6245814	B1	20010612	US 1998-74925	19980508
	US 2002032225	A1	20020314	US 2001-843167	20010427
	CA 2410171	AA	20011220	CA 2001-2410171	20010605
	WO 2001095859	A2	20011220	WO 2001-US17950	20010605
	WO 2001095859	A3	20030828		
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RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR,				

IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN,  
 GW, ML, MR, NE, SN, TD, TG

AU 2001066670	A5	20011224	AU 2001-66670	20010605
EP 1360178	A2	20031112	EP 2001-944241	20010605
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
JP 2004527455	T2	20040909	JP 2002-510041	20010605
US 2003181494	A1	20030925	US 2002-265902	20021008
US 2004186299	A1	20040923	US 2004-808519	20040325
PRAI US 1998-74925	A2	19980508		
US 1999-287237	A2	19990406		
US 2000-591105	A2	20000609		
US 2001-785554	A2	20010220		
US 2001-843167	A	20010427		
WO 2001-US17950	W	20010605		
OS	MARPAT 136:216745			
GI				



AB Title compds. I [wherein Z = G1, H, A2, B2, or G2; n, m, and q = independently 0-4; p = independently 0-5; R, R1, and R2 = independently H, (un)substituted alkyl or alkenyl, CO2Z1, CO2R3, NH2, NHR3, NR32, OH, OR3, or halo; Z1 = H, Na, K, or other pharmaceutically acceptable counterion; R3 = alkyl or alkenyl; A, A1, and A2 = independently H, acylamino, acyloxy, alkanoyl, alkoxy, alkoxy, alkylamino, alkylcarboxylamino, carboxyl, CN, H, or OH; B, B1, and B2 = independently H, acylamino, acyloxy, alkanoyl, alkenoyl, alkoxy, alkylamino, alkylcarboxylamino, aroyl, aralkanoyl, carboxyl, CN, halo, or OH; or A and B or A1 and B1 or A2 and B2 together form a methylenedioxy or ethylenedioxy group; X and X1 = independently NH, NR3, O, or S] are provided which are effective in lowering blood glucose level, serum insulin, triglyceride, and free fatty acid levels in animal models of Type II diabetes. In contrast to previously reported thiazolidinedione

compds., known to lower leptin levels, the present compds. increase leptin levels and have no known liver toxicity. Thus, II was prepared in five steps by condensation of 3,5-dimethoxybenzaldehyde with 4-hydroxyphenylacetic acid (47%), followed by esterification (97%), etherification with 4-fluorobenzaldehyde (77%), condensation with 2,4-thiazolidinedione (86%), and hydrogenation of the ylidene double bond (40%). Oral administration of II to obese mice caused a 62% drop in blood glucose level. I are useful for the treatment of inflammation, inflammatory and immunol. diseases, insulin resistance, hyperlipidemia, coronary artery disease, cancer, and multiple sclerosis.

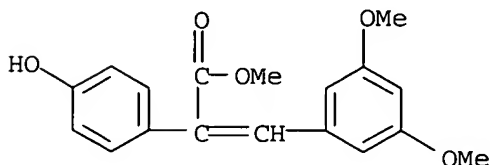
IT 380881-27-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and activity of diphenylethylene thiazolidinediones and analogs as antidiabetics, antiinflammatories, or immunomodulators)

RN 380881-27-6 CAPLUS

CN Benzeneacetic acid,  $\alpha$ -[(3,5-dimethoxyphenyl)methylene]-4-hydroxy-, methyl ester (9CI) (CA INDEX NAME)



L6 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:31392 CAPLUS

DN 136:85656

TI Alpha-arylated cinnamic esters and 1,4-bis( $\alpha$ -carboxyl- $\beta$ -styryl)benzene esters as uv-blocking agents

IN Lakner, Frederick J.; Nag, Bishwajit; Neogi, Partha

PA Calyx Therapeutics, Inc., USA

SO PCT Int. Appl., 16 pp.

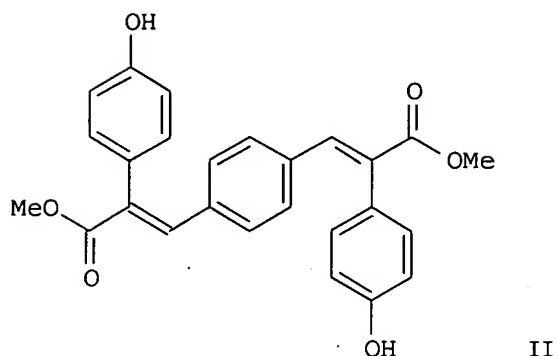
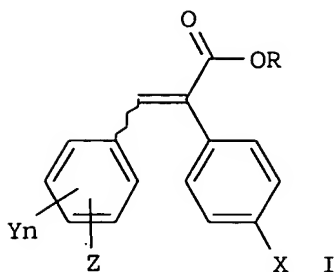
CODEN: PIXXD2

DT Patent

LA English

FAN CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002002501	A1	20020110	WO 2001-US20013	20010622
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	US 6413504	B1	20020702	US 2000-610098	20000630
PRAI	US 2000-610098	A	20000630		
OS	MARPAT 136:85656				
GI					



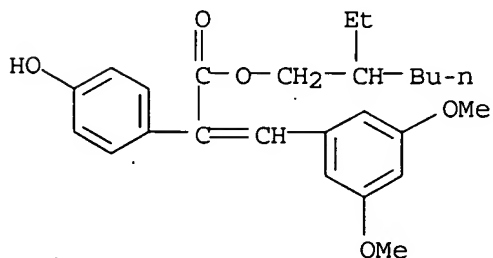
AB Compds. of formula I [R = H, C1-C20 alkyl, or C5-C20 aryl; Z, X, Y = independently H, acylamino, acyloxy, alkoxycarbonyl, amino, C1-C20 alkyl, alkoxy, hydroxy, alkylamino, etc.; n = 1-4] were prepared and their molar extinction coeffs. at 305 nm (UVB radiation) and 350 nm (UVA radiation) were calculated and compared to com. sunscreens. Thus, II was produced via the Perkin condensation of terephthalaldehyde with p-hydroxyphenyl acetic acid followed by esterification with methanol in sulfuric acid.

IT 387354-16-7P

RL: COS (Cosmetic use); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(alpha-arylated cinnamic esters and 1,4-bis(alpha-carboxyl-beta-styryl)benzene esters as uv-blocking agents)

RN 387354-16-7 CAPLUS

CN Benzeneacetic acid,  $\alpha$ -[(3,5-dimethoxyphenyl)methylene]-4-hydroxy-, 2-ethylhexyl ester (9CI) (CA INDEX NAME)

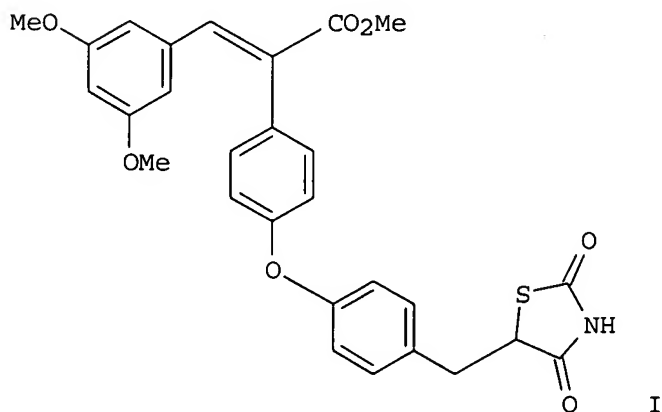


RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 2001:923567 CAPLUS  
DN 136:37596

TI Preparation and activity of diphenylethylene thiazolidinedione or  
 oxazolidinedione compounds as antidiabetics or antiinflammatories  
 IN Neogi, Partha; Nag, Bishwajit; Medicherla, Satyanarayana; Dey,  
 Debendranath  
 PA Calyx Therapeutics, Inc., USA  
 SO PCT Int. Appl., 76 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001095859	A2	20011220	WO 2001-US17950	20010605
	WO 2001095859	A3	20030828		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	US 2002025975	A1	20020228	US 2001-785554	20010220
	US 2002032225	A1	20020314	US, 2001-843167	20010427
	CA 2410171	AA	20011220	CA 2001-2410171	20010605
	AU 2001066670	A5	20011224	AU 2001-66670	20010605
	EP 1360178	A2	20031112	EP 2001-944241	20010605
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR			
	JP 2004527455	T2	20040909	JP 2002-510041	20010605
PRAI	US 2000-591105	A2	20000609		
	US 2001-785554	A2	20010220		
	US 2001-843167	A2	20010427		
	US 1998-74925	A2	19980508		
	US 1999-287237	A2	19990406		
	WO 2001-US17950	W	20010605		
OS	MARPAT 136:37596				
GI					



AB Novel diphenylethylene compds. and derivs. thereof containing  
 thiazolidinedione or oxazolidinedione moieties are provided which are  
 effective in lowering blood glucose level, serum insulin, triglyceride and  
 free fatty acid levels in animal models of Type II diabetes. In contrast

to previously reported thiazolidinedione compds., known to lower leptin levels, the present compds. increase leptin levels and have no known liver toxicity. Thus, (I) was prepared in five steps by condensation of 3,5-dimethoxybenzaldehyde with 4-hydroxyphenylacetic acid followed by esterification and etherification with 4-fluorobenzaldehyde and condensation with 2,4-thiazolidinedione and hydrogenation of the ylidene double bond. Oral administration of I to obese mice caused a 62% drop in blood glucose level. The compds. are disclosed as useful for a variety of treatments including the treatment of inflammation, inflammatory and immunol. diseases, insulin resistance, hyperlipidemia, coronary artery disease, cancer and multiple sclerosis.

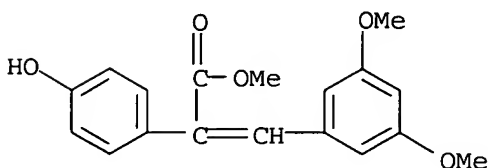
IT 380881-27-6P 380881-43-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and activity of diphenylethylene thiazolidinedione or oxazolidinedione compds. as antidiabetics or antiinflammatories)

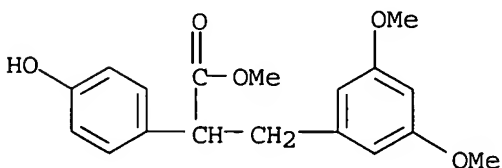
RN 380881-27-6 CAPLUS

CN Benzenecetic acid,  $\alpha$ -[(3,5-dimethoxyphenyl)methylene]-4-hydroxy-, methyl ester (9CI) (CA INDEX NAME)



RN 380881-43-6 CAPLUS

CN Benzenepropanoic acid,  $\alpha$ -(4-hydroxyphenyl)-3,5-dimethoxy-, methyl ester (9CI) (CA INDEX NAME)



L6 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1999:771171 CAPLUS

DN 132:122418

TI Synthesis and biological evaluation of dihydrobenzofuran lignans and related compounds as potential antitumor agents that inhibit tubulin polymerization

AU Pieters, Luc; Van Dyck, Stefaan; Gao, Mei; Bai, Ruoli; Hamel, Ernest; Vlietinck, Arnold; Lemiere, Guy

CS Department of Pharmaceutical Sciences, University of Antwerp, Belgium, B-2610, Belg.

SO Journal of Medicinal Chemistry (1999), 42(26), 5475-5481

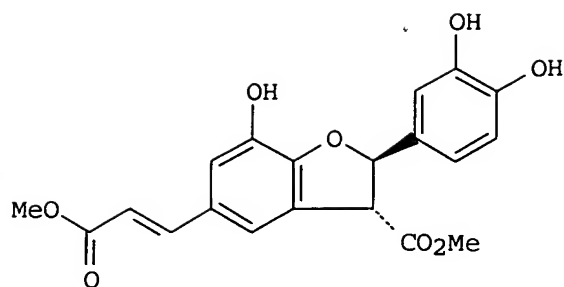
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

GI



I

AB A series of 19 related dihydrobenzofuran lignans and benzofurans was obtained by a biomimetic reaction sequence involving oxidative dimerization of p-coumaric, caffeic, or ferulic acid Me esters, followed by derivatization reactions. All compds. were evaluated for potential anticancer activity in an in vitro human disease-oriented tumor cell line screening panel that consisted of 60 human tumor cell lines arranged in nine subpanels, representing diverse histologies. Leukemia and breast cancer cell lines were relatively more sensitive to these agents than were the other cell lines. Me (E)-3-[2-(3,4-dihydroxyphenyl)-7-hydroxy-3-methoxycarbonyl-2,3-dihydro-1-benzofuran-5-yl]prop-2-enoate (I), the dimerization product of caffeic acid Me ester, containing a 3',4'-dihydroxyphenyl moiety and a hydroxyl group in position 7 of the dihydrobenzofuran ring, showed promising activity. The average GI50 value (the molar drug concentration required for 50% growth inhibition) of I was 0.3  $\mu$ M. Against three breast cancer cell lines, I had a GI50 value of <10 nM. Methylation, reduction of the double bond of the C3-side chain, reduction

of

the methoxycarbonyl functionalities to primary alcs., or oxidation of the dihydrobenzofuran ring to a benzofuran system resulted in a decrease or loss of cytotoxic activity. Compound I inhibited mitosis at micromolar concns. in cell culture through a relatively weak interaction at the colchicine binding site of tubulin. In vitro it inhibited tubulin

polymerization

by 50% at a concentration of  $13 \pm 1 \mu$ M. The 2R,3R-enantiomer of I was twice as active as the racemic mixture, while the 2S,3S-enantiomer had minimal activity as an inhibitor of tubulin polymerization. These dihydrobenzofuran lignans (2-phenyl-dihydrobenzofuran derivs.) constitute a new group of antimitotic and potential antitumor agents that inhibit tubulin polymerization.

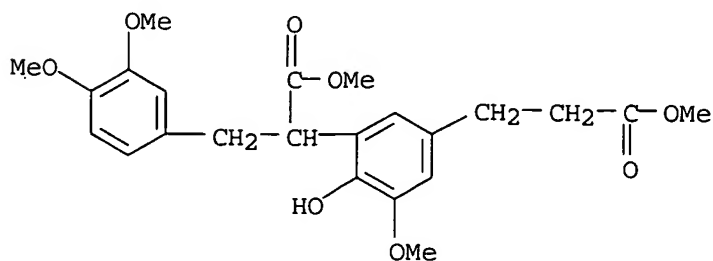
IT 256330-13-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis and biol. evaluation of dihydrobenzofuran lignans and related compds. as potential antitumor agents that inhibit tubulin polymerization)

RN 256330-13-9 CAPLUS

CN Benzenepropanoic acid,  $\alpha$ -[2-hydroxy-3-methoxy-5-(3-methoxy-3-oxopropyl)phenyl]-3,4-dimethoxy-, methyl ester (9CI) (CA INDEX NAME)



RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN  
AN 1980:6338 CAPLUS  
DN 92:6338  
TI Total synthesis of heptamethyl lithospermate  
AU Jacobson, Richard M.; Raths, Richard A.  
CS Dep. Chem., Indiana Univ., Bloomington, IN, 47405, USA  
SO Journal of Organic Chemistry (1979), 44(22), 4013-14  
CODEN: JOCEAH; ISSN: 0022-3263  
DT Journal  
LA English  
GI

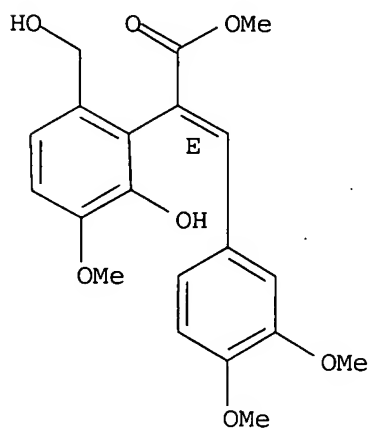
\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -- AVAILABLE VIA OFFLINE PRINT \*

AB 2-Allylisovanillin was reduced with NaBH<sub>4</sub>, acetylated with Ac<sub>2</sub>O, ozonized, and oxidized with H<sub>2</sub>CrO<sub>4</sub> to give 2-acetoxy-6-(acetoxymethyl)-3-methoxybenzeneacetic acid, which was saponified and lactonized (Ac<sub>2</sub>O) to give benzopyranone I. Condensation of I with veratral followed by methanolysis of the lactone and oxidation of the resulting benzyl alc. with (COCl)<sub>2</sub>/Me<sub>2</sub>SO gave aldehyde II. Cyclization of II with HBr gave trans-dihydrobenzofuran III. Doebner condensation of III with malonic acid followed by esterification with Me 3,4-dimethoxyphenyllactate gave heptamethyl lithospermate (IV).

IT 71734-07-1P 71734-08-2P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as intermediate in total synthesis of heptamethyl lithospermate)

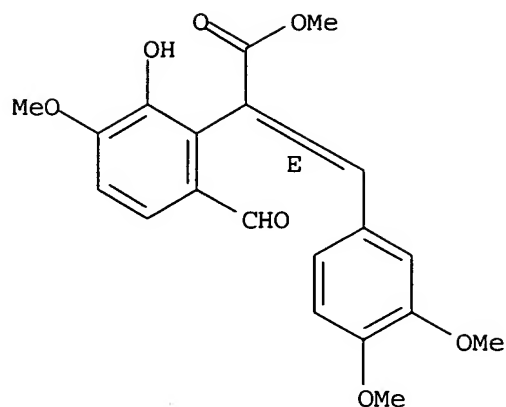
RN 71734-07-1 CAPLUS  
CN Benzeneacetic acid, α-[(3,4-dimethoxyphenyl)methylene]-2-hydroxy-6-(hydroxymethyl)-3-methoxy-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 71734-08-2 CAPLUS  
CN Benzeneacetic acid, α-[(3,4-dimethoxyphenyl)methylene]-6-formyl-2-hydroxy-3-methoxy-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L6 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1963:486261 CAPLUS

DN 59:86261

OREF 59:5096b-h,5097a-e

TI Wilting agents and antibiotics. XXVIII Synthesis of 2,4 dimethoxy 6 hydroxyphenanthrene and constitution of orchinol.

AU Hardegger, E.; Biland, H. R.; Corrodi, H.

CS Eidg. Tech. Hochschule, Zuerich, Switz.

SO Helv. Chim. Acta (1963), 46, 1354-60

DT Journal

LA German

GI For diagram(s), see printed CA Issue.

AB (All m.ps. are corrected). 3,5 (MeO)2C6H3CH2CN [prepared from tech.  $\alpha$ -resorcylic acid via 3,5-(MeO)2C6H3CO2H] (160 g.) refluxed 16 h. with 1.6 l. 20% aqueous KOH and the solution cooled, filtered, extracted with a little Et2O, and acidified with concentrated HCl gave 160 g. 3,5-(MeO)2C6H3CH2CO2H (I), m. 100-1°. I (30 g.) and 30 g. 2,4(O2N)2C6H3CHO dissolved in 300 mL. Ac2O, the solution treated with 21.5 mL. Et3N (the temperature rose to 40-50°), kept 16 h., concentrated in vacuo (H2O pump) at 50-60° to 50-75 mL., treated with 75 mL. H2O at 90° with vigorous shaking, the precipitate filtered off, washed with H2O, dried in vacuo, boiled with 100 mL. C6H6, filtered off while hot, and dried gave 37 g. 2,4 (O2N)2C6H3CH: C[C6H3(OMe)2-3,5]CO2R (II) (R = H), m. 205-6° (C6H6). II (R = H) (3.75 g.) suspended in 200 mL. Et2O treated with Et2OCH2N2 until all solid dissolved and N evolution ceased, the solution evaporated, the residue chromatographed on Al2O3 (activity II),

and

the product eluted with C6H6 gave 3.9 g. II (R = Me), needles, m. 95-6° (Et2O-MeOH); sometimes II (R = Me) was obtained as rhombohedrons, m. 118°; seeding an Et2O solution of the low melting ester with crystals of the higher melting ester gave quant. higher melting ester. II (R = Me) (3.88 g.) in 200 mL. MeOH hydrogenated over 500 mg. 10% Pd-C (after 1 h. and 22 h. 1600 mL. H and 1710 mL. H, resp., was absorbed), the solution filtered, evaporated in vacuo, and the residual oil

(3.3

g.) treated with MeOH gave  $\alpha$ -(3,5 dimethoxyphenyl)- $\beta$ -(2,4 diaminophenyl)propionic acid  $\delta$ -lactam, m. 185° (CHCl3-MeOH); Ac derivative m. 256-8° (CHCl3-MeOH). II (R = H) (10 g.) dissolved in 150 mL. hot AcOH, the solution treated with 18.2 g. SnCl2.2H2O in 30 mL. AcOH at 20° with stirring, saturated with HCl at 0°, stirred 24 h., concentrated in vacuo at 40° to 30 mL., dissolved in 200 mL. Et2O, the solution washed with 7 50-mL. portions H2O until the wash H2O was colorless, extracted with 3 50-mL. portions 2N NaOH, the combined exts. acidified with concentrated HCl, the product isolated with CH2Cl2, dissolved in 50 mL. EtOH, and the solution treated with HCl, the product,  $\alpha$ -(3,5 dimethoxyphenyl) 2 amino 4 nitrocinnamic acid HCl salt (III.HCl), m.

70° (decomposition), filtered off, treated with 150 mL. 1:1 EtOH-H<sub>2</sub>O, the mixture boiled until a clear solution formed, and the solution concentrated to 75

mL. and cooled gave 2.7 g. III, m. 205° (CHCl<sub>3</sub>-MeOH). III treated with CH<sub>2</sub>N<sub>2</sub> in Et<sub>2</sub>O, the product chromatographed on Al<sub>2</sub>O<sub>3</sub> (activity II), and the column eluted with CH<sub>2</sub>Cl<sub>2</sub> and Et<sub>2</sub>O gave Me ester of III, m. 172° (MeOH-CHCl<sub>3</sub>). III (2.4 g.) dissolved in 36 mL. concentrated H<sub>2</sub>SO<sub>4</sub> at -10°, the solution poured on 130 g. ice, treated during 15 min. with 1.45 mL. 5N NaNO<sub>2</sub> at 0° with stirring, stirred 1.5 h., treated with 100 mL. H<sub>2</sub>O, stirred 1.5 h., treated with a small amount of urea (after 0.5 h. HNO<sub>2</sub> was no longer detectable with KI-starch paper), filtered through Celite, the filter cake washed with H<sub>2</sub>O until no reaction with β-naphthol was obtained, the combined filtrates concentrated by boiling 45 min. at 100°, the precipitate filtered off, esterified with CH<sub>2</sub>N<sub>2</sub>, the product chromatographed on Al<sub>2</sub>O<sub>3</sub> (activity II), and the column eluted with C<sub>6</sub>H<sub>6</sub> gave 1.13 g. 2,4 dimethoxy 6 nitro 10 phenanthrenecarboxylic acid (IV) Me ester (V), m. 198° (C<sub>6</sub>H<sub>6</sub>). V (20 mg.) in 10 mL. MeOH boiled 2 h. with 2 mL. N KOH, diluted with 20 mL. H<sub>2</sub>O, and acidified with a few drops concentrated HCl gave IV, m. 280-1° (decomposition) (CH<sub>2</sub>Cl<sub>2</sub>-MeOH). V (1.04 g.) in 125 mL. THF hydrogenated over 1 g. prerduced 10% Pd-C (after 10 min. 190 mL. H absorbed, after 3 h. 207 mL. H; and finally 228 mL. H after 1 min. after addition of 500 mg. prerduced 10% Pd-C) gave 6-NH<sub>2</sub> analog (VI) of V, m. 147-8° (MeOH). VI (622 mg.) dissolved in 20 mL. concentrated H<sub>2</sub>SO<sub>4</sub> at -10°, the solution poured on 100 g. ice with shaking, the resulting suspension treated during 16 min. with 2.1 rel. N NaNO<sub>2</sub> at 0°, the mixture stirred 2 h. at 0°, diluted with 100 mL. H<sub>2</sub>O, stirred 2 h., treated with urea, stirred 0.5 h. (excess HNO<sub>2</sub> was now destroyed), heated 0.5 h. at 100°, cooled, the precipitate (650 mg.) filtered off, boiled 3 h. with 20 mL. MeOH and 5 mL. H<sub>2</sub>O containing 1 g. KOH, the solution evaporated, the residue dissolved in 20 mL. H<sub>2</sub>O, the solution

acidified

with concentrated HCl, the precipitate filtered off, decarboxylated by boiling 2.5 h.

in 10 mL. quinoline with 100 mg. Cu chromite, the mixture added to 100 mL. 2N HCl, filtered, the filter cake and filtrate extracted with Et<sub>2</sub>O, the combined exts. evaporated, the residual oil (235 mg.) chromatographed on Al<sub>2</sub>O<sub>3</sub> (activity II), the column eluted with C<sub>6</sub>H<sub>6</sub>-Et<sub>2</sub>O, and the product (63 mg.) crystallized from C<sub>6</sub>H<sub>6</sub>-hexane gave 8 mg. 2,4-dimethoxy-6hydroxyphenanthrene (VII), m. 135°. VI (311 mg.) diazotized and the solution of diazonium salt boiled down as above, the precipitate (350 mg.) filtered off, treated in

100

mL. MeOH with excess Et<sub>2</sub>O-CH<sub>2</sub>N<sub>2</sub>, after cessation of N evolution the solution evaporated, the residual oil (378 mg.) chromatographed on Al<sub>2</sub>O<sub>3</sub> (activity II), and the product eluted with C<sub>6</sub>H<sub>6</sub> gave 54 mg. Me 2,4,6-trimethoxy-10-phenanthrenecarboxylate, m. 130-1°, which was saponified and decarboxylated as above and then chromatographed on Al<sub>2</sub>O<sub>3</sub> (activity II) and eluted with C<sub>6</sub>H<sub>6</sub> to give 17 mg. 2,4,6-trimethoxyphenanthrene (VIII), m. 109-10° (hexane). Dehydroorchinol (m. 168-70°) was different from synthetic VIII (m. 136°). Although the m.ps. of dehydroorchinol Me ether (m. 113-14°) and synthetic VIII (m. 109-10°) differed only slightly, the mixed m.p. was depressed by 25-30°. From this, it followed that orchinol (Villa) was 2,4-dimethoxy-7-hydroxy-9,10-dihydrophenanthrene. As a supplement to the synthesis of VII was mentioned another route (see below) which, although not carried to completion, should also lead to VII. 2,3,5,6-Br(MeO)<sub>2</sub>(O<sub>2</sub>N) C<sub>6</sub>HCHO (29 g.) dissolved in 900 mL. hot Ac<sub>2</sub>O, the solution treated with 30.5 g. p-HOC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>CO<sub>2</sub>H and 14 mL. Et<sub>3</sub>M at 20°, kept 6 h. at 95-100° with periodic shaking, concentrated in vacuo to 50 mL., heated to 90° with 50 mL. H<sub>2</sub>O, evaporated in vacuo, the residual solid dried 6 h. in vacuo, heated to boiling with 150 mL. C<sub>6</sub>H<sub>6</sub>, and the solution filtered and evaporated gave 20.2 g. 2,3,5,6-Br(MeO)<sub>2</sub>(O<sub>2</sub>N) C<sub>6</sub>HCH:C(C<sub>6</sub>H<sub>4</sub>OR-4)CO<sub>2</sub>R' (IX) (R = R' = H) (X), m. 263-6° (slight decomposition above 230°) (dioxane). X (3 g.) suspended in 200 mL. MeOH treated with

Et<sub>2</sub>O-CH<sub>2</sub>N<sub>2</sub> (all solid dissolved) gave IX (R = H, R' = Me), m. 210-11° (MeOH) X (4.3 g.) in a little H<sub>2</sub>O treated portionwise during 1 h. with 18 mL. 4N KOH and 3.8 g. Me<sub>2</sub>SO<sub>4</sub> at 100° with stirring in such a way that the mixture always remained alkaline, the whole stirred 0.5 h. at 100°, diluted with H<sub>2</sub>O, filtered, and the filtrate acidified with. 2N HCl gave 3.5 g. IX (R = Me, R' = H), m. 224° (EtOHCCl<sub>4</sub>). X (3.47 g.) in 100 mL. EtOH refluxed 21 h. with 3 g. K<sub>2</sub>CO<sub>3</sub> and 2.5 mL. PhCH<sub>2</sub>Cl, the solution filtered, evaporated, the residue dissolved

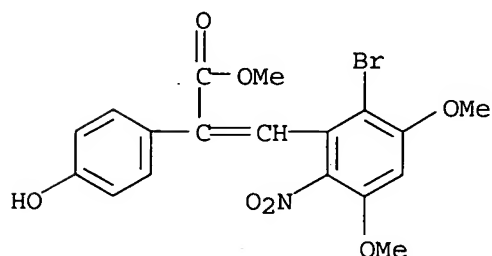
in

300 mL. N Na<sub>2</sub>CO<sub>3</sub>, the solution washed with Et<sub>2</sub>O, brought to pH 1-2 with concentrated HCl, and the product isolated with CHCl<sub>3</sub> gave 1.8 g. IX (R = PhCH<sub>2</sub>, R' = H), m. 2357° (CHCl<sub>3</sub>-MeOH), which was treated in 1:1 MeOH-Me<sub>2</sub>CO with Et<sub>2</sub>O-CH<sub>2</sub>N<sub>2</sub> to give IX (R = PhCH<sub>2</sub>, R' = Me), m. 187° (Et<sub>2</sub>O-petr. ether).

IT 93870-75-8, Acrylic acid, 3-(2-bromo-3,5-dimethoxy-6-nitrophenyl)-2-(p-hydroxyphenyl)-, methyl ester  
(preparation of)

RN 93870-75-8 CAPLUS

CN Acrylic acid, 3-(2-bromo-3,5-dimethoxy-6-nitrophenyl)-2-(p-hydroxyphenyl)-, methyl ester (7CI) (CA INDEX NAME)



L6 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1963:428381 CAPLUS

DN 59:28381

OREF 59:5094g-h,5095a-h,5096a-b

TI Wilting agents and antibiotics. XXVII. Induced defensive substances in the Orchidaceae. 2

AU Hardegger, E.; Schellenbaum, M.; Corrodi, H.

CS Eidg. Tech. Hochschule, Zuerich, Switz.

SO Helvetica Chimica Acta (1963), 46, 1171-80

CODEN: HCACAV; ISSN: 0018-019X

DT Journal

LA German

GI For diagram(s), see printed CA Issue.

AB Biol. investigations have shown that under the influence of certain moribific agents, defensive substances are produced in the corms of Orchidaceae; e.g., the mycorrhizal fungus Rhizoctonia repens activates defense mechanisms in the corms of Orchis militaris, which clearly result in the formation of orchinol (I), C<sub>16</sub>H<sub>16</sub>O<sub>3</sub>, as the sole defensive substance, along with biol. inactive p-HOC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>OH (II); both I and II are not found in healthy plants. However, Loroglossum hircinum produces no I, but other defensive substances against R. repens. From infected corms of L. hircinum was isolated a biol. inactive compound, C<sub>16</sub>H<sub>16</sub>O<sub>3</sub>, designated lorroglossol (III), isomeric with and closely related to I. (All m.ps. are corrected). The Et<sub>2</sub>Oeluate (loc. cit.) chromatographed again on Al<sub>2</sub>O<sub>3</sub> (activity II) gave II, m. 120° (MeOH-H<sub>2</sub>O), mol. weight (camphor) 136. p-HOC<sub>6</sub>H<sub>4</sub>CO<sub>2</sub>Me (10 g.) in 150 mL. Et<sub>2</sub>O added dropwise to 6 g. LiAlH<sub>4</sub> in 100 mL. Et<sub>2</sub>O at 20° with stirring, the whole refluxed 3 h., decomposed with EtOAc and H<sub>2</sub>O under ice cooling, acidified with AcOH, and the product isolated with Et<sub>2</sub>O gave 2 g. II, m. 122° (H<sub>2</sub>O). I (20

$\gamma$ ) in 20  $\mu$ l. MeOH applied to Whatman Number 1 paper, the solution allowed to travel with 1:1 MeOH-H<sub>2</sub>O, the paper dried, sprayed with 0.1% alc. N,2,6 trichloro-p-benzoquinone imine, followed by saturated aqueous borax, and dried gave a grayish green spot corresponding to I with R<sub>f</sub> 0.56; I had R<sub>f</sub> 0.79 with 1:1 EtOH-H<sub>2</sub>O. EtOH-Et<sub>2</sub>O-exts. of infected corm fragments of *L. hircinum* were prepared and worked up in a manner similar to the isolation of I from the corms of *O. militaris* to give III, m. 98° (C<sub>6</sub>H<sub>6</sub>-cyclohexane, then MeOH). III (50 mg.), 0.1 mL. Me<sub>2</sub>SO<sub>4</sub>, and 140 mg. K<sub>2</sub>CO<sub>3</sub> in 10 mL. Me<sub>2</sub>CO refluxed 22 h., cooled, filtered, the filtrate evaporated, the residue (52 mg.) chromatographed on Al<sub>2</sub>O<sub>3</sub> (activity I), and the column eluted with CH<sub>2</sub>Cl<sub>2</sub> gave 27 mg. Me ether of III, b<sub>0.1</sub> 200°. I (20 mg.) and 93 mg. 3,5(O<sub>2</sub>N)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>COCl in 1 mL. absolute pyridine kept 30 min. at 20°, boiled 2 min., cooled, diluted with 20 mL. Et<sub>2</sub>O, filtered, the filtrate washed with dilute HCl, saturated aqueous KHCO<sub>3</sub>, and saturated salt solution, dried, and evaporated gave 30 mg. I 3,5 dinitrobenzoate, m. 198° (CH<sub>2</sub>Cl-Et<sub>2</sub>O). A solution of 500 mg. I, 1.9 g. p-MeC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>Cl (IIIa), and 5 mL. pyridine was prepared at 0°, kept 24 h. at 20°, treated with 1 mL. H<sub>2</sub>O, kept 1 h., taken up in CHCl<sub>3</sub>, and the solution washed (dilute HCl, saturated aqueous KHCO<sub>3</sub>, and H<sub>2</sub>O) and evaporated to give 774 mg. I tosylate (IV), oil which crystallized, m. 101-3° (MeOH-H<sub>2</sub>O). IV (50 mg.) and 25 mg. NaI in Me<sub>2</sub>CO or in Ac<sub>2</sub>O refluxed 5 h. gave (from each experiment) quant. unchanged IV. IV (100 mg.) and 100 mg. LiAlH<sub>4</sub> in 5 mL. dioxane refluxed 2 h., treated with EtOAc and H<sub>2</sub>O to destroy excess LiAlH<sub>4</sub>, acidified with AcOH, and the product isolated with Et<sub>2</sub>O (the extract was washed in the usual manner) gave 59 mg. I after crystallization from C<sub>6</sub>H<sub>6</sub>-cyclohexane. Saponification of IV with dilute aqueous NaOH also gave I. I (300 mg.) in 6 mL. Et<sub>2</sub>O and 21 mL. 2% Et<sub>2</sub>O-CH<sub>2</sub>N<sub>2</sub> kept 12 h. at 20°, the solution filtered, evaporated, the residue chromatographed on Al<sub>2</sub>O<sub>3</sub> (activity II), and the column eluted with C<sub>6</sub>H<sub>6</sub> gave 51 mg. Me ether (V) of I, m. 86-7° (cyclohexane); continued elution with 1:1 C<sub>6</sub>H<sub>6</sub>-Et<sub>2</sub>O gave 213 mg. unchanged I. I (340 mg.) stirred to a paste with a little H<sub>2</sub>O, the paste treated during 1 h. with alternate portions of 2.3 mL. 4N KOH (total) and 0.37 mL. Me<sub>2</sub>SO<sub>4</sub> (total) at 100° in such a way that the mixture always remained alkaline, kept 30 min. at 100°, cooled, filtered, the filtrate extracted with C<sub>6</sub>H<sub>6</sub>, the extract washed, evaporated, and the residue purified as above gave 298 mg. V, m. 86-7°. To 128 mg. I in 2 mL. AcOH was added dropwise 80 mg. Br in 1 mL. AcOH and the solution poured into H<sub>2</sub>O to give di-Br derivative of I, m. 154° (CCl<sub>4</sub>). To 200 mg. I in 4 mL. CHCl<sub>3</sub> and 10 mL. CCl<sub>4</sub> was added dropwise during 30 min. 9 mL. 0.18 M CCl<sub>4</sub>-Br at 0°, the solution stirred 30 min. (no more free Cl was present) evaporated in vacuo, the residue (265 mg.) adsorbed on silica gel, the chromatogram developed with C<sub>6</sub>H<sub>6</sub>CHCl<sub>3</sub>, the column extruded, and the visible zones sectioned and eluted with CHCl<sub>3</sub> to give 153 mg. di-Cl derivative of I, m. 133-40° (unsharp) (C<sub>6</sub>H<sub>6</sub>-cyclohexane, then sublimation in vacuo), and 63 mg. tri-Cl derivative of I, m. 198-9° (C<sub>6</sub>H<sub>6</sub>-cyclohexane, then sublimation in vacuo); the former compound migrated slower than the latter compound IV (750 mg.) in 60 mL. EtOH hydrogenated at atmospheric pressure over 4 g. fresh prerduced Raney Ni W-2, the hydrogenation continued (2 addns. of 2 g. fresh catalyst were made) (after 3 days 128 mL. H was absorbed), the solution filtered, evaporated, the partially crystalline residue dissolved in C<sub>6</sub>H<sub>6</sub>, the solution washed with H<sub>2</sub>O, evaporated, the residue (286 mg.) chromatographed on Al<sub>2</sub>O<sub>3</sub> (activity I), and the column eluted with C<sub>6</sub>H<sub>6</sub> gave 1st 58 mg. oil and then 228 mg. deoxyorchinol (VI), C<sub>16</sub>H<sub>16</sub>O<sub>2</sub>, m. 58-9° (pentane). VI (170 mg.) and 510 mg. pyridine-HCl heated 6 h. at 210-20°, the mixture partitioned between Et<sub>2</sub>O-2N HCl, and the

Et2O-layer washed (H2O and 2N NaOH) and evaporated gave 11 mg. neutral oily fraction; the NaOH-soluble product (135 mg.) chromatographed on silica gel and the product eluted with Et2O gave 117 mg. deoxydidemethylorcinol (VII), m. 145° (C6H6). o- (VIII) and pC6H4(OH)2 (IX) and VII (5 mg. each) in absolute Et2O and in absolute C6H6 were boiled 5 min. with 500 mg.

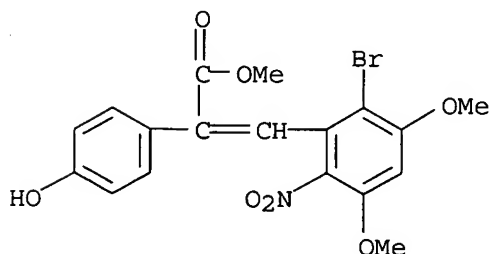
Ag2O

and kept overnight. VIII and IX gave instantaneous red and yellow colors, resp., with Et2O (even at 20°). VII did not give these color reactions. VII (100 mg.) and 0.2 mL. Ac2O in 1 mL. pyridine kept 12 h. at 20° and poured into ice H2O gave 117 mg. VII diacetate, m. 92-3° (C6H6-petr. ether). VII (75 mg.) and 665 mg. IIIa in 2 mL. pyridine kept 12 h. at 20° and worked up as was IV gave 173 mg. VII ditosylate, m. 163° (C6H6-Et2O). I (500 mg.) and 75 mg. 10% Pd-C heated 5 min. at 180-200° (34 mL. H obtained), the product chromatographed on Al2O3 (activity II), and the column eluted with 1:1 C6H6-Et2O gave 266 mg. dehydroorcinol (X), C16H14O3, m. 168-70° (C6H6). X (100 mg.) methylated with 0.11 mL. Me2SO4 and 0.7 mL. 4N KOH as above, the product chromatographed on Al2O3 (activity II), and the column eluted with 1:1 C6H6-petr. ether gave 94 mg. X Me ether (XI), m. 113-14°. V (540 mg.) and 80 mg. 10% Pd-C heated 5 h. at 210-80° (31 mL. H obtained), the product chromatographed on Al2O3 (activity II), eluted with C6H6-petr. ether, and recrystd. from C6H6-petr. ether gave 340 mg. XI, m. 111-13°; unchanged V remained in the mother liquor. VII (250 mg.) and 40 mg. 10% Pd-C heated 5 h. at 250-300° (6 mL. H and an undetd. amount H2O obtained), the petr. ethersol. fraction of the dehydrogenation product chromatographed on Al2O3 (activity I), and the column eluted with petr. ether gave 54 mg. phenanthrene, m. 94-5° (EtOH) [trinitrobenzene complex m. 158° (EtOH)]; the petr. ether insol. fraction recrystd. from C6H6-petr. ether gave 2 phenanthrol, m. 163-4° [acetate m. 139-40° (C6H6-petr. ether)]. VI (300 mg.) and 45 mg. 10% Pd-C heated 1 h. at 260-80° (21 mL. H obtained), the C6H6-soluble fraction of the dehydrogenation product chromatographed on Al2O3 (activity I), and the product eluted with 1:1 C6H6-petr. ether and repeatedly recrystd. from cyclohexane gave 146 mg. deoxydehydroorcinol (XII), C16H14O2, m. 75-6°, identical (mixed m.p. and UV and IR spectra) with 2,4 dimethoxyphenanthrene. XII (107 mg.) and 320 mg. pyridine-HCl heated 6 h. at 210-20°, the product (CHCl3-soluble, H2O-insol.) extracted with 2N NaOH, the extract acidified, the resulting oil (77 mg.) acetylated with Ac2O in pyridine, and this product chromatographed in silica gel and eluted with Et2O gave 52 mg. di O acetyldeoxydehydrodidemethylorcinol (XIII), m. 128-30°. These results indicated that I was either 2,4 dimethoxy 6 or 7 hydroxy 9,10 dihydrophenanthrene (XIV). The UV spectrum (EtOH) of I and the IR spectra (KBr) of I and XII were recorded.

IT 93870-75-8, Acrylic acid, 3-(2-bromo-3,5-dimethoxy-6-nitrophenyl)-2-(p-hydroxyphenyl)-, methyl ester  
(preparation of)

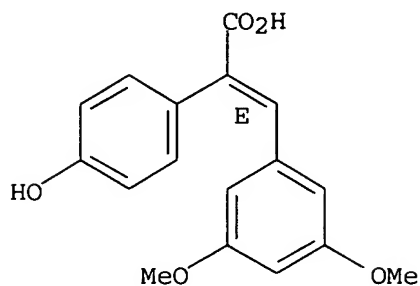
RN 93870-75-8 CAPLUS

CN Acrylic acid, 3-(2-bromo-3,5-dimethoxy-6-nitrophenyl)-2-(p-hydroxyphenyl)-, methyl ester (7CI) (CA INDEX NAME)



L2 ANSWER 6 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN

Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

CN Benzeneacetic acid,  $\alpha$ -[(3,5-dimethoxyphenyl)methylene]-4-hydroxy-,  
( $\alpha$ E)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Benzeneacetic acid,  $\alpha$ -[(3,5-dimethoxyphenyl)methylene]-4-hydroxy-,  
(E) -

L2 ANSWER 7 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

CN Insulin (9CI) (CA INDEX NAME)

OTHER NAMES:

CN Actrapid

CN Actrapid HM

CN Actrapid MC

CN Decurvon

CN Dermulin

CN Endopancrine

CN Exubera

CN HMR 4006

CN Iletin

CN Insular

CN Insulin Injection

CN Insulyl

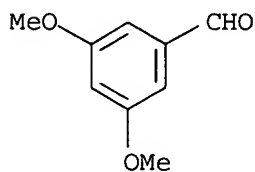
CN Intesulin B

CN Iszilin

CN Mixtard

CN Musulin

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\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

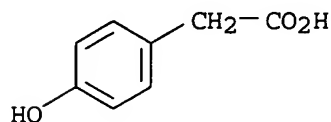
CN Benzaldehyde, 3,5-dimethoxy- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

OTHER NAMES:

CN 3,5-Dimethoxybenzaldehyde

CN NSC 62667

L2 ANSWER 9 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

CN Benzeneacetic acid, 4-hydroxy- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Acetic acid, (p-hydroxyphenyl)- (8CI)

OTHER NAMES:

CN (4-Hydroxyphenyl)acetic acid

CN (p-Hydroxyphenyl)acetic acid

CN 2-[4-(Hydroxy)phenyl]acetic acid

CN 4-(Carboxymethyl)phenol

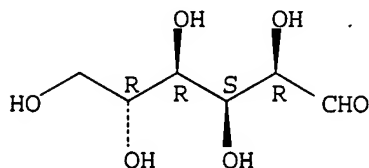
CN 4-Hydroxybenzeneacetic acid

CN NSC 25066

CN NSC 27460

L2 ANSWER 10 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

CN D-Glucose (8CI, 9CI) (CA INDEX NAME)

OTHER NAMES:

CN (+)-Glucose

CN Anhydrous dextrose

CN Cartose

CN Cerelose

CN Cerelose 2001

CN Clearsweet 95

CN Clintose L

CN Corn sugar

CN CPC hydrate

CN D(+)-Glucose

CN Dextropur

CN Dextrose

CN Dextrosol

CN Glucodin

CN Glucolin

CN Glucose

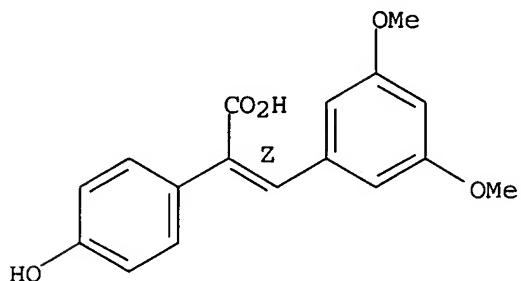
CN Glucosteril  
CN Goldsugar  
CN Grape sugar  
CN Maxim Energy Gel  
CN Meritose  
CN Meritose 200  
CN Roferose ST  
CN Staleydex 111  
CN Staleydex 130  
CN Staleydex 333  
CN Staleydex 95M  
CN Sugar, grape  
CN Tabfine 097(HS)  
CN Vadex

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L2 ANSWER 1 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN

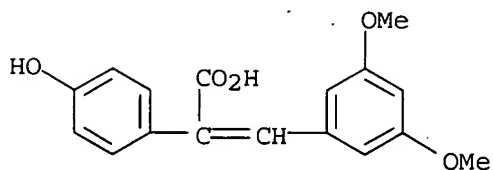
Double bond geometry as shown.



● Na

CN Benzeneacetic acid,  $\alpha$ -[(3,5-dimethoxyphenyl)methylene]-4-hydroxy-, monosodium salt, ( $\alpha$ Z)- (9CI) (CA INDEX NAME)

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\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

CN Benzeneacetic acid,  $\alpha$ -[(3,5-dimethoxyphenyl)methylene]-4-hydroxy-, (9CI) (CA INDEX NAME)

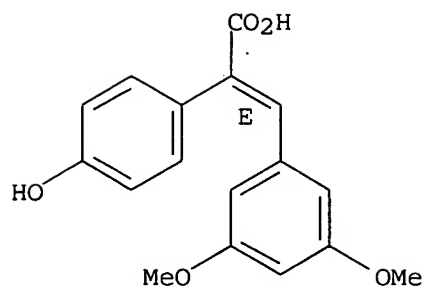
OTHER NAMES:

CN 3-(3,5-Dimethoxyphenyl)-2-(4-hydroxyphenyl)acrylic acid

CN NSC 613734

L2 ANSWER 3 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN

Double bond geometry as shown.

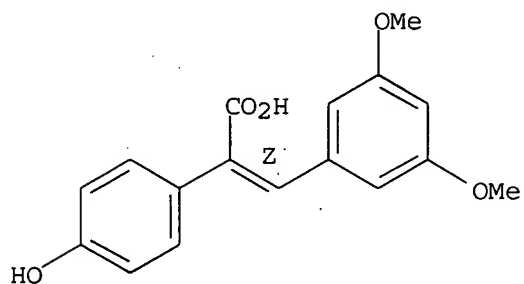


● Na

CN Benzeneacetic acid,  $\alpha$ -[(3,5-dimethoxyphenyl)methylene]-4-hydroxy-, monosodium salt, ( $\alpha$ E)- (9CI) (CA INDEX NAME)

L2 ANSWER 4 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN

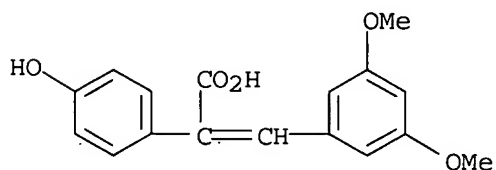
Double bond geometry as shown.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

CN Benzeneacetic acid,  $\alpha$ -[(3,5-dimethoxyphenyl)methylene]-4-hydroxy-, ( $\alpha$ Z)- (9CI) (CA INDEX NAME)

L2 ANSWER 5 OF 10 REGISTRY COPYRIGHT 2005 ACS on STN



● Na

CN Benzeneacetic acid,  $\alpha$ -[(3,5-dimethoxyphenyl)methylene]-4-hydroxy-, monosodium salt (9CI) (CA INDEX NAME)